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| 10/090,347 | 03/04/2002 | Peter H. Tang | | 3959 |

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EXAMINER

NOGUEROLA, ALEXANDER STEPHAN

ART UNIT PAPER NUMBER

1753

DATE MAILED: 12/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/090,347

Applicant(s)

TANG ET AL.

Examiner

ALEX NOGUEROLA

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 August 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10 and 12-19 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10, 12 and 19 is/are rejected.
- 7) ☒ Claim(s) 13-18 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 04 March 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Response to Amendment

1. Applicants' amendment of August 20, 2004 does not render the application allowable.

Response to Arguments

2. Applicant's arguments filed August 20, 2004 have been fully considered but they are not persuasive. With respect to the rejection of claims 10-12 (new claim 10 now has the limitation of previous claim 11) as being anticipated by Matson, Applicants assert that Matson does not teach (1) the analysis of electrochemically reversible compounds, and (2) using a voltage of +700 mV in the guard cell. As for analyzing electrochemically reversible compounds, the examiner respectfully submits that Matson does teach this feature. Matson states, "[t]he technique disclosed herein also may be advantageously used for producing coulometric cells for specific ions ... for example ... for PO₄ measurement, or ... for sulfate measurement." See

col. 8, ll. 5-10. Phosphate and sulfate engage in electrochemically reversible reactions. See "Chemical of the Week – Phosphoric acid, H₃ PO₄", "Diagram of the Sulfur Cycle", and "Sulfur Cycle Lecture Outline". As for using a voltage of +700 mV in the guard cell, Matson only *mentions* using a voltage of -500 mV (col. 7, ll. 41-46), but since the purpose of the guard cell is to suppress background signals by removing or modifying electroactive contaminants (col. 7,

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ll. 41-46 and col. 2, ll. 45-55), barring a showing of evidence to the contrary, such as unexpected results, the voltage choice is just optimization. That is, it would have been obvious to use +700 mV instead of - 500 mV if +700 mV would remove or modify the worst of the contaminants. Alternatively, it would have been obvious to use +700 mV in a second guard cell (Figure 6; col. 7, l. 5-10) to remove additional contaminants to those removed by a first guard cell using - 500 mV or some other voltage. The examiner though has reconsidered the statutory basis of the rejection. Claims 10 and 12 are now rejected under 35 U.S.C. §103(a).

Status of the Objections and Rejections Pending since the Office action of June 02, 2004

3. All claim objections are withdrawn.
4. All rejections under 35 U.S.C. § 112, second paragraph, are withdrawn.
5. The rejections of claims 1-9 and 11 as being anticipated under 35 U.S.C. §102(b) by Matson are withdrawn as these claims have been cancelled.
6. The rejections of claims 10 and 12 as being obvious under 35 U.S.C. §102(b) over Matson are withdrawn, but have been newly rejected under 35 U.S.C. 103(a).

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7. The Declaration under 37 CFR 1.132 (inadvertently labeled as 37 C.F.R. 1.131), by Peter Tang, filed July 15, 2004 is sufficient to overcome the rejection of claims 1-17 based upon Tang I (*Clinical Chemistry* 47:2, 258-265 February 01, 2001). Declarations under 37 CFR 1.132 by Michael Miles and Ton de Grauw were also submitted to the examiner on November 17, 2004.

8. The rejections of claims 1-9 being obvious under 35 U.S.C. §103(a) over Tang II are withdrawn as these claims have been cancelled.

Claim Rejections - 35 USC § 112

9. Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention:

Claim 10 recites the limitation "said sample solution" in line 13. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

10. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

11. Claims 10, 12, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Matson (US 4,552,013), hereafter "Matson."

Addressing claim 10, Matson teaches a method for simultaneously analyzing an electrochemically reversible material (col. 8, ll. 5-19¹) comprising the steps of

- a) passing the materials through a liquid chromatographic column for achieving time-spaced separation of the materials from the column (Figure 1 and col. 7, ll. 27-38)²;
- a) oxidizing the materials by passing the materials through a coulometric guard cell (abstract; Figure 1; and col. 7, ll. 16-26);
- b) passing the materials through an analytical cell consisting essentially of a series of at least two coulometric electrodes (col. 7, ll. 38-41)³;

¹ Matson states, "[t]he technique disclosed herein also may be advantageously used for producing coulometric cells for specific ions ... for example ... for PO₄ measurement, or ... for sulfate measurement." See col. 8, ll. 5-10. Phosphate and sulfate engage in electrochemically reversible reactions. See "Chemical of the Week - Phosphoric acid, H₃PO₄", "Diagram of the Sulfur Cycle", and "Sulfur Cycle Lecture Outline".

² "Unless the steps of a method actually recite an order, the steps are not ordinarily construed to require one. However, such a result can ensue when the method steps implicitly require that they be performed in the order written. In this case, nothing in the claim or the specification directly or implicitly requires such a narrow construction." *Interactive Gift Express, Inc. v. Compuserve Inc.* 59 USPQ2d 1401, 1416 (citations omitted).

the at least two coulometric electrodes being arranged in series and defining collectively at least one flow channel for the sample solution (col. 7, ll. 38-41)⁴.

Although Matson does not mention analyzing a mixture, it would have been obvious to do so because the system of Matson is clearly configured for mixtures as it includes a chromatography column (col. 7, ll. 36-41). Furthermore, Matson also discloses that several measurement electrodes may be provided so that different substances may be detected (col. 7, ln. 60 – col. 8, ln. 4).

As for using a voltage of +700 mV in the guard cell, Matson only *mentions* using a voltage of –500 mV (col. 7, ll. 41-46), but since the purpose of the guard cell is to suppress background signals by removing or modifying electroactive contaminants (col. 7, ll. 41-46 and col. 2, ll. 45-55), barring a showing of evidence to the contrary, such as unexpected results, the voltage choice is just optimization. That is, it would have been obvious to one with ordinary skill in the art at the time of the invention to use +700 mV instead of – 500 mV if +700 mV would remove or modify the worst of the contaminants. Alternatively, it would have been obvious to use +700 mV in a second guard cell (Figure 6; col. 7, l. 5-10) to remove additional contaminants to those removed by a first guard cell using – 500 mV or some other voltage.

Addressing claim 12, Matson does not mention the claimed voltages for the coulometric guard cell and the electrodes in the analytical cell; however, barring evidence to the contrary, such as unexpected results, especially since the sample has not been specified, the

³ ESA Inc., *ibid*.

⁴ *Ibid*.

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voltages used are just a matter of optimizing the method, which was within the skill of one with ordinary skill in the art at the time of the invention. The voltage in the coulometric guard cell will depend on the background material to be removed (col. 6, ll. 47-62; col. 7, ll. 41-46; and col. 2, ll. 45-55) and voltages for the electrodes in the analytical cell will depend on the analyte(s) to be detected.

Addressing claim 19, Matson does not *mention* a solution derived from solid matrices such as tissues, cell lysates and solid pharmaceutical formulations. It would have been obvious to one with ordinary skill in the art at the time of the invention to consider deriving a solution from such matrices because Matson discloses detecting and measuring glycosides, polypeptides, sugars, and phosphatides. See col. 8, ll. 10-19. Also, that the solution is derived from the claimed solid matrices does not limit the actual composition of the solution. Broadly interpreted, a solution of simple salts may be derived from a solid matrix such as tissue.

Allowable Subject Matter

12. Claims 13-18 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

13. The following is a statement of reasons for the indication of allowable subject matter:

a) Claim 13 requires the mixture to comprise quinones and hydroquinones in a biological fluid. Matson does not disclose detecting and measuring quinones or hydroquinones in a biological fluid. Matson discloses directly measuring inorganic ions such as phosphate and sulfate and indirectly measuring biological compounds by providing immobilized enzymes and electrically conductive ion exchange resins to give enhanced selectivity to biological compounds such as glycosides, polypeptides, sugars, and phosphatides, which are not chemically similar to quinones or hydroquinones. See col. 8, l. 5-19. By using enzymes when biological compounds in a mixture are to be measured the first and second electrodes in the analytical cell would not detect and measure the electrochemically reversible materials in the sample, as required by claim 10, from which claim 13 ultimately depends, but instead the first and second electrodes in the analytical cell would detect and measure electrochemically reversible (possibly) products of the enzymatic reaction on the biological materials in the sample.

b) Claims 14-17 depend directly or indirectly from allowable claim 13;

c) Claim 18 requires using Coenzyme Q₉ as an internal standard. This implies measuring and detecting Coenzyme Q₉ or a similar compound. Matson discloses directly measuring inorganic ions such as phosphate and sulfate and indirectly measuring biological compounds by providing immobilized enzymes and electrically conductive ion exchange resins to give enhanced selectivity to biological compounds such as glycosides,

polypeptides, sugars, and phosphatides, which are not chemically similar to quinones or hydroquinones. See col. 8, l. 5-19. By using enzymes when biological compounds in a mixture are to be measured the first and second electrodes in the analytical cell would not detect and measure the electrochemically reversible materials in the sample, as required by claim 10, from which claim 18 depends, but instead the first and second electrodes in the analytical cell would detect and measure electrochemically reversible (possibly) products of the enzymatic reaction on the biological materials in the sample.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEX NOGUEROLA whose telephone number is (571) 272-1343. The examiner can normally be reached on M-F 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, NAM NGUYEN can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Alex Noguerola
Primary Examiner
AU 1753
November 18, 2004